Policy Number	OTH903.043
Policy Effective Date	09/15/2026

Brolucizumab-dbll

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Disclaimer

Medical policies are a set of written guidelines that support current standards of practice. They are based on current generally accepted standards of care developed by: nonprofit professional association(s) for the relevant clinical specialty, third-party entities that develop treatment criteria, or other federal or state governmental agencies. A requested therapy must be proven effective for the relevant diagnosis or procedure. For drug therapy, the proposed dose, frequency and duration of therapy must be consistent with recommendations in at least one authoritative source. This medical policy is supported by FDA-approved labeling and/or nationally recognized authoritative references to major drug compendia, peer reviewed scientific literature and generally accepted standards of medical care. These references include, but are not limited to: MCG care guidelines, DrugDex (IIa level of evidence or higher), NCCN Guidelines (IIb level of evidence or higher), NCCN Compendia (IIb level of evidence or higher), professional society guidelines, and CMS coverage policy.

Carefully check state regulations and/or the member contract.

Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Legislative Mandates

EXCEPTION: For members residing in the state of Ohio, § 3923.60 requires any group or individual policy (Small, Mid-Market, Large Groups, Municipalities/Counties/Schools, State Employees, Fully-Insured, PPO, HMO, POS, EPO) that covers prescription drugs to provide for the coverage of any drug approved by the U. S. Food and Drug Administration (FDA) when it is prescribed for a use recognized as safe and effective for the treatment of a given indication in one or more of the standard medical reference compendia adopted by the United States Department of Health and Human Services or in medical literature even if the FDA has not approved the drug for that indication. Medical literature support is only satisfied when safety and efficacy has been confirmed in two articles from major peer-reviewed professional medical journals that present data supporting the proposed off-label use or uses as generally safe and effective. Examples of accepted journals include, but are not limited to, Journal of

American Medical Association (JAMA), New England Journal of Medicine (NEJM), and Lancet. Accepted study designs may include, but are not limited to, randomized, double blind, placebo controlled clinical trials. Evidence limited to case studies or case series is not sufficient to meet the standard of this criterion. Coverage is never required where the FDA has recognized a use to be contraindicated and coverage is not required for non-formulary drugs.

Coverage

Intravitreal injections of brolucizumab-dbll (Beovu®) **may be considered medically necessary** for the following indications:

- Diabetic macular edema;
- Treatment of neovascular (wet) age-related macular degeneration.

Intravitreal injections of brolucizumab-dbll (Beovu®) **are considered experimental, investigational and/or unproven** for all other non-Food and Drug Administration approved ophthalmological indications.

Policy Guidelines

Brolucizumab-dbll (Beovu®) is contraindicated in patients with ocular or periocular infections, as well as active intraocular inflammation.

Description

Vascular endothelial growth factor (VEGF) is a protein in the body that stimulates the growth of new blood vessels needed for healing, such as when the body has sustained an injury. (2) In certain diseases in the eye, such as wet macular degeneration and macular edema, VEGF encourages the growth of abnormal blood vessels underneath the retina, as well as causing direct damage to existing blood vessels. These abnormal and/or damaged blood vessels are prone to breaking and leaking fluid and blood into the retina. The fluid that has leaked into the retina leads to swelling of the retinal cells, damage to the retina, and consequently, vision loss. Anti-VEGF medications stop VEGF production in order to reduce the threat of vision loss. Brolucizumab-dbll (Beovu®) is one of a number of anti-VEGF medications.

Regulatory Status

Brolucizumab-dbll (Beovu®) is a human VEGF inhibitor and was approved by the U.S. Food and Drug Administration (FDA) in 2019 for the treatment of neovascular (wet) age-related macular degeneration (AMD). In 2022, the FDA approved brolucizumab-dbll for diabetic macular edema. (3)

Rationale

This policy is based on the U.S. Food and Drug Administration (FDA) labeled indications for brolucizumab-dbll (Beovu®).

Brolucizumab-dbll (Beovu®) (1)

Neovascular (Wet) Age-Related Macular Degeneration (AMD)

The safety and efficacy of Beovu were assessed in two randomized, multi-center, double-masked, active-controlled studies (HAWK - NCT02307682 and HARRIER - NCT02434328) in patients with neovascular AMD. A total of 1817 patients were treated in these studies for two years (1088 on brolucizumab and 729 on control). Patient ages ranged from 50 to 97 years with a mean of 76 years.

In the HAWK study, patients were randomized in a 1:1:1 ratio to the following dosing regimens:
1) brolucizumab 3 mg administered every 8 or 12 weeks after the first 3 monthly doses;
2) brolucizumab 6 mg administered every 8 or 12 weeks after the first 3 monthly doses;
3) aflibercept 2 mg administered every 8 weeks after the first 3 monthly doses.

In the HARRIER study, patients were randomized in a 1:1 ratio to the following dosing regimens:
1) brolucizumab 6 mg administered every 8 or 12 weeks after the first 3 monthly doses;
2) aflibercept 2 mg administered every 8 weeks after the first 3 monthly doses.

In both studies, after three initial monthly doses (Week 0, 4, and 8), treating physicians decided whether to treat each individual patient on a every 8 week or 12-week dosing interval guided by visual and anatomical measures of disease activity, although the utility of these measures has not been established. Patients on 12-week dosing intervals could be changed based on the same measures to an 8-week schedule after subsequent treatment visits. Any patient placed on an 8-week schedule, remained on the 8-week dosing interval until the end of the study. Protocol-specified visits in the initial three months occurred every 28 ± 3 days followed by every 28 ± 7 days for the remainder of the studies. Baseline anatomical measures may have contributed to the regimen selection because the majority of patients on the 12-week dosing schedule at the end of the trial had less baseline macular edema and/or smaller baseline lesions.

Both studies demonstrated efficacy in the primary endpoint defined as the change from baseline in Best Corrected Visual Acuity (BCVA) at Week 48, measured by the Early Treatment Diabetic Retinopathy Study (ETDRS) Letter Score. In both studies, Beovu treated patients had a similar mean change from baseline in BCVA as the patients treated with aflibercept 2 mg (fixed every 8 weeks). Detailed results of both studies are shown in Table 1 and figures 1 and 2 below.

Table 1. Efficacy Outcomes at Week 48 and 96 in Phase 3 HAWK and HARRIER Studies

		HAWK			HARRIER		
Efficacy outcome	**At Week**	**Beovu (n=360)**	**Aflibercept 2 mg (n=360)**	**Difference (95% CI)**	**Beovu (n=370)**	**Afliber-cept**	**Difference (95% CI) brolucizu-**

				brolucizumab aflibercept		2 mg (n=369)	mab aflibercept
Mean (SD) BCVA at Baseline	---	60.8 (13.7)	60.0 (13.9)	---	61.5 (12.6)	60.8 (12.9)	---
Mean (SE) change from baseline in BCVA (measured by ETDRS letters score)	48	6.6 (0.71)	6.8 (0.71)	-0.2 (-2.1, 1.8)	6.9 (0.61)	7.6 (0.61)	-0.7 (-2.4, 1.0)
	96	5.9 (0.78)	5.3 (0.78)	+0.5 (-1.6, 2.7)	6.1 (0.73)	6.6 (0.73)	-0.4 (-2.5, 1.6)
Proportion of patients who gained visual acuity (%) (> 15 letters of BCVA)	48	33.6	25.4	8.2 (2.2, 5.0)	29.3	29.9	-0.6 (-7.1, 5.8)
	96	34.2	27	7.2 (1.4, 3.8)	29.1	31.5	-2.4 (-8.8, 4.1)
Proportion of patients who lost visual acuity (%) (> 15 letters of BCVA)	48	6.4	5.5	0.9 (-2.7, 4.3)	3.8	4.8	-1.0 (-3.9, 2.2)
	96	8.1	7.4	0.7 (-3.6, 4.6)	7.1	7.5	-0.4 (-3.8, 3.3)

Abbreviations - BCVA: Best Corrected Visual Acuity; missing data are imputed using last observation carried forward (LOCF) method, ETDRS: Early Treatment Diabetic Retinopathy Study, SE: standard error, WK: week, CI: confidence interval.

Figure 1. Mean Change in Visual Acuity From Baseline to Week 96 in HAWK

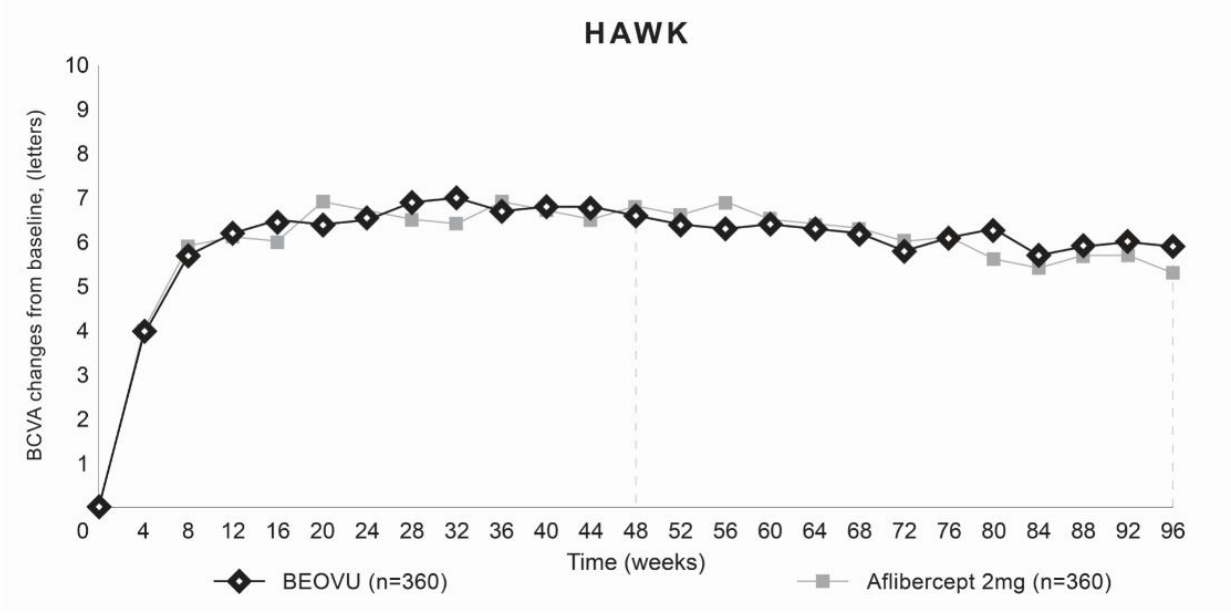
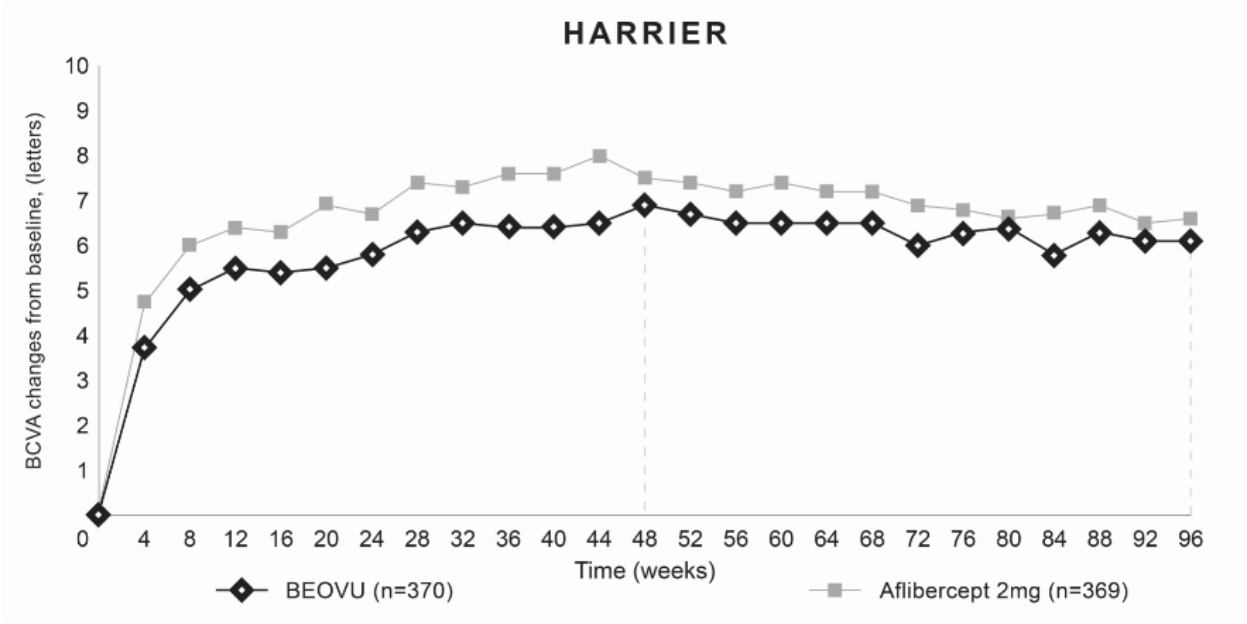


Figure 2. Mean Change in Visual Acuity From Baseline to Week 96 in HARRIER



Through Week 48, 56% (HAWK) and 51% (HARRIER) of patients remained on Beovu every 12 weeks. The proportion of patients who were maintained on every 12-week dosing through Week 96 was 45% and 39% in HAWK and HARRIER, respectively. The probability of remaining on every 12-week dosing from Week 20 to Week 48 was 85% and 82%, and from Week 48 to Week 96 was 82% and 75% in HAWK and HARRIER, respectively.

Treatment effects in evaluable subgroups (e.g., age, gender, race, baseline visual acuity) in each study were generally consistent with the results in the overall populations.

Diabetic Macular Edema (DME)

The safety and efficacy of Beovu were assessed in two randomized, multi-center, double-masked, active controlled studies (KESTREL – NCT03481634 and KITE - NCT03481660) in patients with DME. A total of 926 patients were treated in these studies for 1 year (558 on brolucizumab and 368 on aflibercept 2 mg). Patient ages ranged from 23 to 87 years with a mean of 63 years.

In KESTREL, patients were randomized in a 1:1:1 ratio to the following dosing regimens:

1) brolucizumab 6 mg administered once every 6 weeks for first 5 doses, followed by brolucizumab 6 mg every 8 or 12 weeks;
2) brolucizumab 3 mg administered once every 6 weeks for first 5 doses, followed by brolucizumab 3 mg every 8 or 12 weeks;
3) aflibercept 2 mg administered once every 4 weeks for first 5 doses, followed by aflibercept 2 mg every 8 weeks.

In KITE, patients were randomized in a 1:1 ratio to the following dosing regimens:

1) brolucizumab 6 mg administered once every 6 weeks for first 5 doses, followed by brolucizumab 6 mg every 8 or 12 weeks;
2) aflibercept 2 mg administered once every 4 weeks for first 5 doses, followed by aflibercept 2 mg every 8 weeks.

In both studies, after the first five doses (Weeks 0, 6, 12, 18 and 24), brolucizumab patients were treated every 12 weeks, with the option of adjusting to an every 8 week dosing interval based on disease activity. Disease activity was assessed by changes in visual acuity and/or anatomical parameters, including central retinal subfield thickness (CST) and/or presence of intraretinal fluid (IRF)/subretinal fluid (SRF) although the utility of the specific action parameters used has not been established. Disease activity was assessed by a physician during the first 12-week interval (at Weeks 32 and 36) and at each subsequent scheduled 12-week treatment visit. Patients who showed disease activity at any of these visits were adjusted to an every 8 week treatment interval. The comparator aflibercept was administered every 8 weeks after the first 5 monthly doses.

The primary efficacy endpoint for both studies was the change from baseline to Week 52 in Best Corrected Visual Acuity (BCVA) as measured by the Early Treatment Diabetic Retinopathy Study (ETDRS) Letter Score with the primary objective being to demonstrate non-inferiority of Beovu vs. aflibercept 2 mg. In both studies, Beovu was non-inferior to aflibercept 2 mg for the change in BCVA from baseline to Week 52 and the change from baseline over the period Week 40 through Week 52.

After 5 initial q6w loading doses, the patients in the Beovu arm could have received between the minimum of 2 and maximum of 3 additional injections through Week 52. At Week 52, the median number of injections given over 12 months was 7 in patients treated with Beovu.

Through Week 52, 55% (KESTREL) and 50% (KITE) of patients remained on Beovu every 12 weeks. The probability of remaining on every 12-week dosing from Week 36 to Week 52 was 88% and 95% in KESTREL and KITE, respectively. Results of both studies are shown in Table 2 and figures 3 and 4 below.

Table 2. Efficacy Outcomes at Week 52 in Phase 3 – KESTREL and KITE Studies

		KESTREL			KITE		
Efficacy outcome	**At Week**	**Beovu (n=189)**	**Aflibercept 2 mg (n=187)**	**Difference (95% CI) Beovu-aflibercept**	**Beovu (n=179)**	**Aflibercept 2 mg (n=181)**	**Difference (95% CI) Beovu-aflibercept**
Change from baseline in BCVA (measured by ETDRS letters score) – LS mean (SE)	52	9.2 (0.57)	10.5 (0.57)	-1.3 (-2.9, 0.3)	10.6 (0.66)	9.4 (0.66)	1.2 (-0.6, 3.1)
	40-52	9.0 (0.53)	10.5 (0.53)	-1.5 (-3.0, 0.0)	10.3 (0.62)	9.4 (0.62)	0.9 (-0.9, 2.6)

BCVA: Best Corrected Visual Acuity; CI: confidence interval; ETDRS: Early Treatment Diabetic Retinopathy Study; n: number(s).
BCVA assessments after start of alternative DME treatment in the study eye were censored and replaced by the last value prior to start of this alternative treatment.

Figure 3. Mean Change in Visual Acuity from Baseline to Week 52 in KESTREL

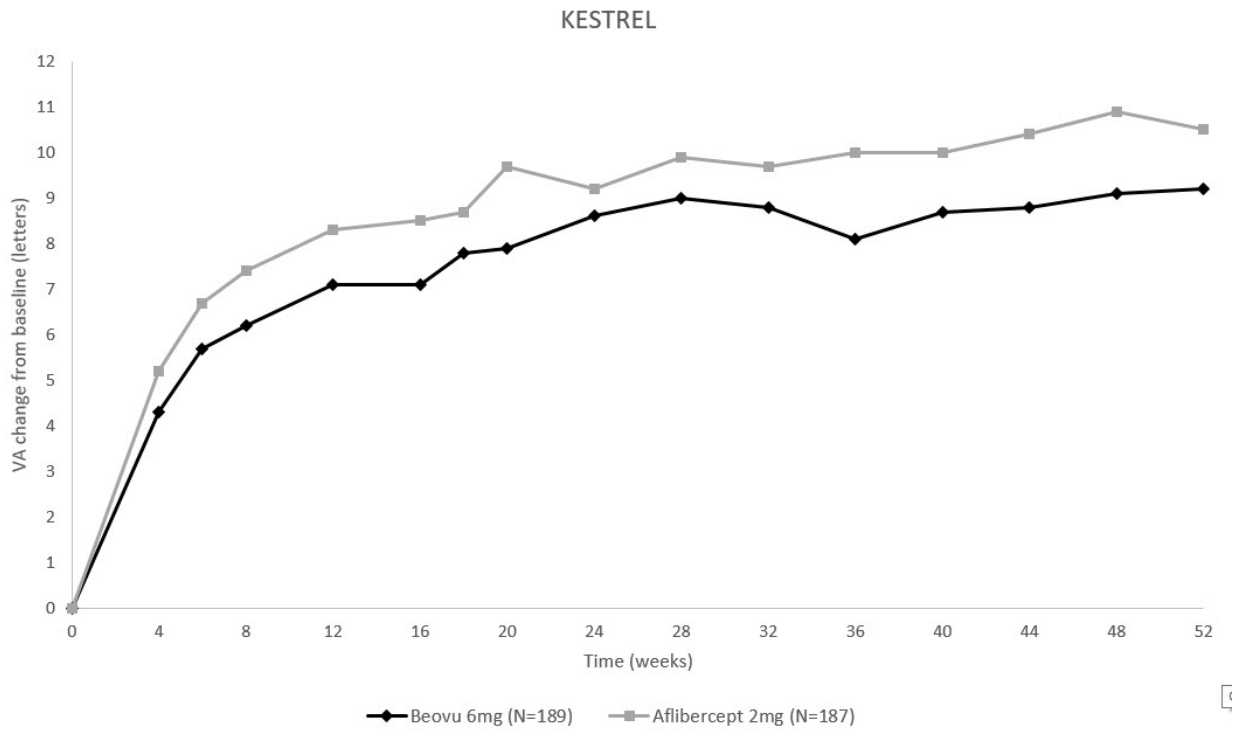
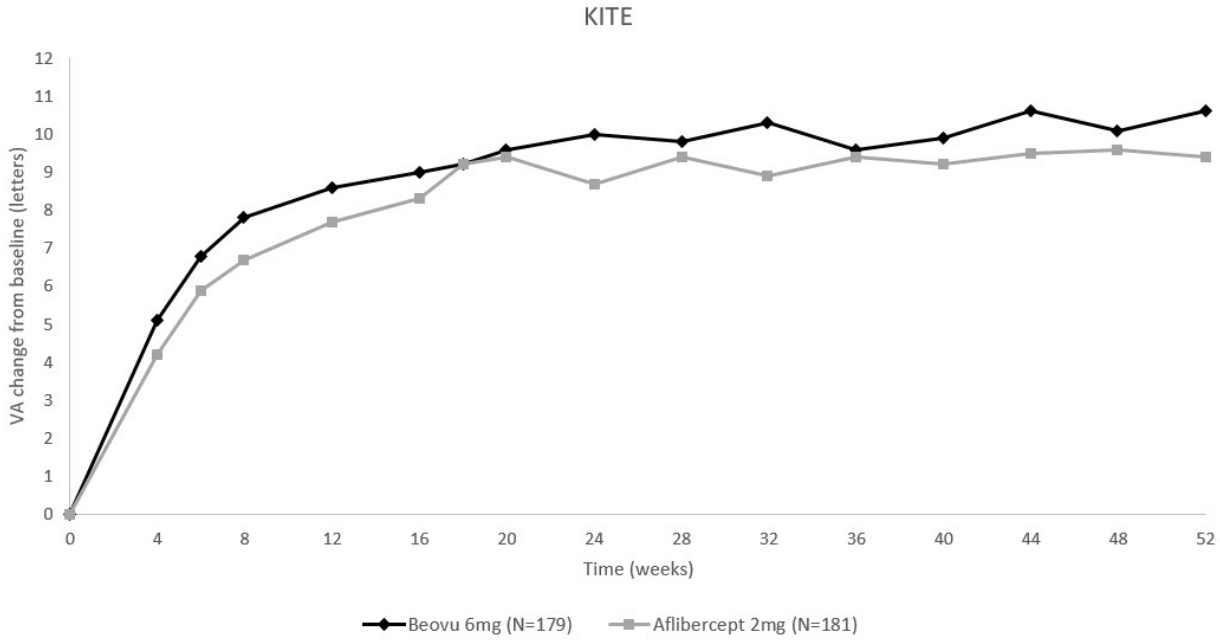


Figure 4. Mean Change in Visual Acuity from Baseline to Week 52 in KITE



Treatment effects in evaluable subgroups (i.e., age, gender, baseline HbA1c, baseline visual acuity, baseline central subfield thickness, DME lesion type, duration of DME since diagnosis, retinal fluid status) in each study were generally consistent with the results in the overall population.

In both studies, Beovu demonstrated a significant reduction from baseline in CST starting at Week 4 and continuing up to Week 52.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	67028
HCPCS Codes	J0179

*Current Procedural Terminology (CPT®) ©2025 American Medical Association: Chicago, IL.

References

U.S. Food and Drug Administration Label

1. FDA. Highlights of Prescribing Information Beovu® (brolucizumab-dbll). Revised 7/2024. Available at: <https://www.accessdata.fda.gov> (accessed on December 11, 2025).

Other

2. Lazarus R. How Do Anti-VEGF Injections Work? Available at <https://www.optometrists.org> (accessed December 11, 2025).
3. Beovu FDA Approval History. Available at <https://www.drugs.com> (accessed December 11, 2025).

Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision

Date	Description of Change
09/15/2026	Reviewed. No changes.
01/01/2026	Document updated. Document updated. Document updated. The following changes were made to Coverage: 1) Removed both Avastin step-therapy and continuation therapy language; 2) Modified list of conditionally covered indications; 3) Modified experimental, investigational and/or unproven statement to include “non-Food and Drug Administration approved”. Added reference 2 and 3; reference 1 updated.
02/01/2025	Document updated. The following change was made to Coverage: Added language regarding drug shortages/recalls to “Initial Therapy” criteria. No new references added.
05/15/2024	Document updated. The following change was made to Continuation Therapy in Coverage for brolucizumab-dbll (Beovu®): removed “through a previously authorized pharmacy or medical benefit” in the statement “Continuation of brolucizumab-dbll (Beovu®) therapy may be considered medically necessary for all members (including new members…” Now reads: Continuation of brolucizumab-dbll (Beovu®) therapy may be considered medically necessary for all Members (including new members): who are currently receiving the requested medication, AND who are experiencing benefit from therapy as evidenced by disease stability or disease improvement, AND when dosing is in accordance with an authoritative source.” No new references added.
10/01/2023	Document updated. The following change was made to Coverage: Added preferred criteria for bevacizumab (Avastin™). No new references added.
06/01/2023	Document updated with literature review. Coverage unchanged. No new references added; one updated.
07/15/2022	New medical document. Intravitreal injections of brolucizumab-dbll (Beovu®) as an anti-VEGF (vascular endothelial growth factor) therapy, may be considered medically necessary for the following indications: Diabetic macular edema; Treatment of neovascular (wet) age-related macular degeneration (AMD); Treatment of choroidal neovascularization (CNV; includes myopic CNV or mCNV) due to: Angioid streaks, Central serous chorioretinopathy, Choroidal retinal neovascularization, secondary to pathologic myopia, Choroidal retinal neovascularization, degenerative progressive high myopia, Choroidal rupture or trauma, Idiopathic choroidal neovascularization, Multifocal choroiditis, Pathologic myopia, Presumed ocular histoplasmosis syndrome, and Uveitis. Intravitreal injections of brolucizumab-dbll (Beovu®) as an anti-VEGF (vascular endothelial growth factor) therapy are considered experimental, investigational and/or unproven for all other ophthalmological indications. Brolucizumab-dbll (Beovu®) was previously addressed on OTH903.020 Intravitreal Angiogenesis Inhibitors for Choroidal Vascular Conditions.